

Exhibit A
Amendments to the Specification showing Insertions and Deletions

Page 4, line 10, with amendments shown:

--Methods and compounds are provided for multiplexed determinations, where the compounds can be linked to binding compounds for detection of reciprocal binding compounds in a sample. The methods are distinguished by having a plurality of binding events in a single vessel using a mixture of differentially eTag reporter [~~receptor~~] conjugated binding compounds, the release of identifying eTag reporter [~~receptor~~] of those binding compounds bound to their target compounds in the same vessel, and the detection of the released identifying tags by separation of the tags in a single run. The eTag reporter [~~receptor~~] are distinguished by having one or more physical characteristics that allow them to be separated and detected.

The method employs a mixture of binding compounds bound to eTag reporters, where each eTag reporter has a characteristic that allows it to be uniquely detected in a single separation run. The method involves combining the eTag reporter conjugated binding compound with a sample to determine the presence of a plurality of targets under conditions where the binding compounds bind to any reciprocal binding partners to form a binding complex. After sufficient time for binding to occur, the eTag reporters can be released from binding complexes in the same vessel. Various techniques are employed depending upon the nature of the binding compounds for releasing the eTag reporters bound to the complex. The released eTag reporters are then separated and identified by their differentiable characteristics free of interference from the eTag reporters still bound to the binding compound. The techniques for differentiating between eTag reporters bound to a complex and not bound to a complex, include enzymatic reactions that require the complex to exist for cleavage to occur, modification by using ligand/receptor binding, where the ligand is part of the binding compound, so that after cleavage, eTag reporter [~~receptor~~] still bound to the binding compound is modified, dual binding to the target resulting in release of the eTag reporter [~~receptor~~], where optionally eTag reporter [~~receptor~~] bound to the binding compound is modified, and the like.

One set of eTag reporters [~~receptors~~] are distinguished by differences, which include mass as a characteristic. These eTag reporters do not rely on differentiation based on oligonucleotides of 2 or more, usually 3 or more nucleotides, but rather on organic chemical building blocks that are conveniently combined together to provide for large numbers of differentiable compounds. Therefore, while the original eTag reporter or eTag reporter

conjugated to the binding compound can have 2 or more nucleotides, when released from the binding compound, the released eTag reporter will have not more than 3, usually not more than 2 nucleotides. Of particular interest are eTag reporters [~~receptors~~] that are characterized by differences in their mass/charge ratio. These compounds are distinguished by having differences in mobility and are characterized by having regions, which serve as (1) a cleavable linking region; (2) a mass-modifying region; (3) a charge-modifying region; and (4) a detectable region, where the regions may be separate and distinct or combined, there being at least two distinct regions that provide for the differentiation. These eTag reporters may be combined in kits and assays with compounds having all of the regions within a single region to further expand the number of different compounds used as eTag reporters in a multiplexed determination. These compounds find use with other compounds where the different regions are present in the same moiety, for example one to two regions, where the charge-modifying region may also be the detectable region or the mass-modifying region. By having a plurality of compounds that can serve as identifying molecules, mixtures of target compounds can be assayed in a single vessel. By using protocols that result in the release of eTagTM reporters from the binding compound that are identifiable due to differences in mobility, the analysis is greatly simplified, since the eTag reporters will be substantially free of interfering materials and their differences in mobility will allow for accurate detection and quantitation.—

Page 4, lines 12-13, with amendments shown:

--The kits include sets of e-tag probes, a [~~epature~~] capture agent and [~~optionally~~] optionally a cleaving [~~agnet~~] agent.--

Page 5, lines 13-14, with amendments shown:

--Figure 4 illustrates the design and synthesis of e-tags using [~~a LabCard (Detection: 4.7 em; 200 V/cm) and~~] standard phosphoramidite coupling chemistry.—

Page 7, lines 20-21, with amendment shown:

--Figure 33 is a schematic diagram of the steps involved in the synthesis of the phosphoroamidite of biotin-deoxycytosine (dC)[~~(Reagent C)~~].—

Page 7, lines 22-23, with amendment shown:

--Figure 34 is a schematic diagram of the steps involved in the synthesis of the phosphoroamidite of biotin-deoxyadenosine (dA)[~~(Reagent D)~~].--

Page 26, lines 13-19, with amendments shown:

-- In one approach, the e-tag probe is constructed sequentially from a single or several monomeric phosphoramidite building blocks (one containing a dye residue), which are chosen to generate tags with unique electrophoretic mobilities based on their mass to charge ratio. The e-tag probe is thus composed of monomeric units of variable charge to mass ratios bridged by phosphate linkers. Figure 4 illustrates the design and synthesis of e-tags using [~~a LabCard~~ (~~Detection: 4.7 cm; 200 V/cm~~) and] standard phosphoramidite coupling chemistry.[~~}]~~ The separation of e-tags on a LabCard (Figure 5) has been demonstrated.--